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Title: Interpersonal processes in Paranoia: A systematic review

Running head: Interpersonal processes in paranoia

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ABSTRACT

Paranoid ideation is a core feature of psychosis, and models of paranoia have long proposed that it arises in the context of disturbances in the perception of the self. However, to develop targeted interventions, there is benefit in clarifying further which aspects of self perception are implicated. Interpersonal sensitivity is a personality trait which has been associated with the risk of paranoid thinking in the general population. However, not all studies have found this link. We aimed to review the empirical literature assessing the association between interpersonal sensitivity and paranoia in both general population and clinical samples; and to explore if associations found differed depending on whether state or trait paranoia was assessed. The review followed PRISMA guidelines. Articles were identified through a literature search in OVID (PsychINFO, MEDLINE) and Web of Science up to December 2016. Fourteen studies with a total of 12,138 participants were included. All studies were of 'fair' or 'good' quality. A robust association was found between interpersonal sensitivity and paranoia in clinical and general population samples alike, regardless of method of assessment of both paranoia and interpersonal sensitivity. Although this finding was more pronounced in studies of trait paranoia, it is likely that differences in study purpose, measurement and power explain these differences. Findings from this review support the hypothesis that feelings of personal vulnerability and exaggerated socially evaluative concerns are central for both onset and maintenance of paranoid symptoms, suggesting avenues for future research in targeted interventions.

Keywords: Paranoia, interpersonal sensitivity, self, interpersonal processes, psychosis, systematic review

INTRODUCTION

Paranoid ideation, the unfounded belief that others have hostile intentions and want to cause personal harm (Garety and Freeman, 2013) is a core feature of psychosis, prevalent in over 70% of those presenting with a first episode of psychosis (Coid et al., 2013). Paranoid ideation is likely caused by the misinterpretation of internal arousal and states (Freeman et al., 2005) and it has also been observed in people suffering from other mental health disorders like anxiety disorders, particularly social anxiety disorder (Gilbert et al., 2005; Michail and Birchwood, 2009), depression (Wigman et al., 2012; Fusar-Poli et al., 2014), and dementia (Selbæk et al., 2013). However, previous research suggests that paranoid thinking is not a distinct emotional state common to those with mental health difficulties, but that it is exponentially distributed in the population; meaning 'that many individuals have few paranoid thoughts, and few individuals have many' (Freeman et al., 2005). Paranoia occurs on a single dimension, with social evaluative concerns on one end of the continuum and persecutory delusions on the other (Freeman et al., 2005). Findings from general population-based studies indicate that as many as 30% of people regularly have paranoid thoughts, and about 5% have experienced persecutory thinking (Johns et al., 2004; Freeman et al., 2011; Bebbington et al., 2013); albeit in only in a minority this is persistent enough to prompt help-seeking (Freeman et al., 2011).

Furthermore, there is strong evidence that factors associated with paranoid thinking are the same among clinical and non-clinical populations; for example attachment disruptions (Pickering et al., 2008), childhood trauma (Reininghaus et al., 2016), particularly bullying (Bentall et al., 2012; Valmaggia et al., 2015), and growing up in an urban environment (Freeman et al., 2015) have all been found to increase the risk for paranoid ideation. Overall, paranoia has been associated with lower physical and psychological wellbeing, mood, and social inclusion; causing significant levels of distress, disability and reductions in psychological functioning (Freeman et al., 2011; Freeman and Garety, 2014; Gilbert et al., 2005).

Perceptions of the self have long been hypothesised to be one important feature in the development and maintenance of paranoid thinking. For example, early psychoanalytic theories conceptualised paranoia as serving a defensive function (Freud, 1911), which was expanded on more recently by Bentall and colleagues (Bentall, 1994; Bentall and David, 2003; Udachina et al., 2017). They propose that individuals with paranoia make external, other-blaming causal attributions for negative events; thereby preserving self-esteem and deflecting feelings of low self-worth. According to this theory, individuals with paranoia have positive explicit (observable) self-esteem, but negative implicit (subconscious) self-esteem. Bentall and colleagues (2001) propose that by making external causal attributions, the individual diminishes the discrepancy between perceptions of the "real self" (who

the person is) and the “ideal self” (who the person feels he/she ought to be). Therefore, paranoia serves as a defence of the self, which is implicitly experienced as weak and defective.

In contrast, cognitive models of paranoia propose that severe adverse childhood effects create enduring negative beliefs about the self as vulnerable and the world as being hostile, which, in turn, is related to emotional distress and paranoid ideation (Garety et al., 2001).

Studying the self in relation to paranoia is an area of considerable complexity. Three recent reviews have explored the research in this area more widely (Kesting and Lincoln, 2013; Freeman and Garety, 2014; Tiernan et al., 2014). Freeman & Garety (2014) concluded that there is convincing evidence for the association of persecutory delusions and negative self-thoughts, and point out that this finding also fits with the wider literature on associations of negative emotions and positive symptoms of psychosis, as well as with evidence for the social defeat hypothesis of psychosis (Selten and Cantor-Graee, 2005; Valmaggia et al., 2015).

Tiernan et al. (2014) conducted a narrative review of eighteen studies on the relationship of self-concepts and paranoia. Paranoia was consistently associated with more negative self-concepts in cross-sectional studies, but findings were more mixed with regard to discrepancies in self-concept, and the dimensional aspects of self-concept and paranoia; with explicit and implicit self-concepts being more negative in clinical than in non-clinical groups, but with normal or higher self-esteem when persecution was seen as undeserved. These findings mirror those from a systematic review by Kesting and Lincoln (2013) on self-esteem and persecutory delusions which included 52 studies. The authors also concluded that global explicit self-esteem is lower, and self-schemas are more negative in those with persecutory delusions, and that higher self-esteem was associated with lower perceived deservedness. Therefore, both reviews conclude that there is little support for Bentall and colleagues’ (2001) ‘paranoia as defence’ theory, but that data to date are more likely to support cognitive models of paranoia.

Interpersonal sensitivity is a personality trait related to low self-esteem and negative self-concepts, which has gained increasing attention in the literature. Interpersonally sensitive individuals place *“an undue and excessive awareness of, and sensitivity to, the behaviour and feelings of others... particularly to perceived or actual situations of criticism or rejection...”* (Boyce and Parker, 1989). Therefore, they are highly vigilant to other’s expectations of them, fearful of negative evaluation, and will modify their behaviour to minimise the risk of social rejection; to the point of personal avoidance and non-assertive behaviour. The construct of interpersonal sensitivity encompasses: interpersonal awareness, fragile inner self, need for approval, separation anxiety, and timidity (Boyce and Parker, 1989).

First shown to be both a consequence of, and a vulnerability to depression (Boyce et al., 1991; Wilhelm et al., 2004), interpersonal sensitivity has been associated with the onset of persecutory delusions in both high risk for psychosis (Masillo et al., 2012) and general population samples (Freeman et al., 2005c; Green et al., 2008). It has been hypothesised that the belief that the self is vulnerable, bothersome, and has to be hidden from others feeds into paranoid experiences via several different routes, for example via the ability to develop and maintain social contacts (Maki et al., 2005; Gayer-Anderson and Morgan, 2013), or by using maladaptive coping strategies to resolve interpersonal conflict (Bak et al., 2003; Lin et al., 2011). However, other studies have been less clear on the relationship with overall interpersonal sensitivity and paranoia (Freeman et al., 2008; Valmaggia et al., 2007); although they have commonly found associations with at least one of its components (interpersonal awareness, fragile inner self, need for approval, separation anxiety, and timidity).

It is possible that differences in the definition and measurement of paranoia have contributed to the differences in findings. Some studies focused on ascertaining whether paranoia can be 'triggered' in a 'neutral' situation (e.g. Freeman et al., 2008); thus, focusing on measuring a 'state paranoia' and its correlations with interpersonal sensitivity; whereas other studies investigated associations with a more enduring and stable paranoia-proneness; defined as 'trait paranoia' (e.g. Masillo et al. 2012).

Given that this is a relatively new area of research, to date, there has been no systematic review of the literature exploring whether high levels of interpersonal sensitivity or one of its components are associated with paranoia in both general population and clinical samples. Similarly, no review has explored whether outcomes differ depending on whether 'state' or 'trait' paranoia was investigated.

The aim of this study was therefore to systematically review the evidence on interpersonal sensitivity and paranoia to answer the following questions:

- i) Is there an association between interpersonal sensitivity, including high levels of interpersonal awareness, a fragile inner self, need for approval, separation anxiety, timidity and paranoia in both general population and clinical samples?
- ii) Is the quality of these relationships different depending on whether state or trait paranoia was assessed?

METHODS

A review of the literature was performed following PRISMA guidelines (Moher et al., 2016). The literature review was registered on PROSPERO (registration number: PROSPERO 2016:CRD42016053765) in December 2016.

Literature search

Articles were identified through a literature search in OVID (PsychINFO, MEDLINE) and Web of Science from inception to December 2016.

Inclusion and exclusion criteria

The inclusion criteria were: (1) Original Studies published up to December 2016; (2) Written in English; (3) Using clinical samples with a diagnosis of psychosis, schizophrenia, or related symptoms, those at high risk of these mental health difficulties, or general population samples; (4) young adults (>16 years) or adults; (5) measured interpersonal sensitivity or one of its components, and (6) measured paranoia, a related concept, or group differences in interpersonal sensitivity as outcome measure. We excluded studies which solely focused on attachment or self-esteem, were not focused on interpersonal sensitivity as defined by Boyce & Parker (1989), review studies, conference abstracts, studies not written in English, and studies using samples of children under the age of 16 years.

Search Criteria

We used combinations of the following keywords: (Psychos* OR psychot* OR schizophren* OR paranoi* OR prodrom* OR at risk mental state OR ultra high risk OR hallucinat* OR voice* OR delusio*) AND (interpersonal sensitivity OR rejection sensitivity OR criticism sensitivity OR timidity OR separation anxiety OR affective sensitivity OR interpersonal awareness OR need for approval OR fragile inner self). Additional references were retrieved by cross-referencing of selected articles, and through hand searches. Disagreement was resolved through discussion relevant to the inclusion and exclusion criteria

Quality assessment

We used the quality assessment tools developed by the National Heart Lung and Blood Institute of the National Institutes of Health (NHLBI). We decided on these tools because they cover the wide range

of study designs that would be included in our review, and are not specific to the area of investigation; making them suitable for assessing studies concerned with mental health outcomes. All tools included items to assess the potential for methodological flaws which could constitute sources of bias (e.g. selection, performance, attrition, and detection), confounding, power and other factors. Study quality was assessed by two raters, and discrepancies resolved through discussion. Reviewers answered 'yes', 'no', and 'cannot determine' for each item, based on guidance documents developed for each tool. Each study received an overall rating of 'good', 'fair', or 'poor'. Briefly, 'good' studies had strong methodologies, and low risk of bias, 'fair' studies had some methodological shortcomings which increased the risk of bias, and 'poor' studies had significant methodological flaws which could render results invalid.

RESULTS

As shown in Figure 1, initially, $n = 3911$ hits were identified, and a further eight were identified through hand searches. After removal of duplicates, title and abstract were screened of $n = 2999$ studies. Of those, $n = 2957$ records were excluded ($n = 2608$ after title review, $n = 349$ after abstract review). The full text was accessed of $n = 42$ studies, and $n = 28$ were excluded. Reasons for exclusion were: investigating self-esteem or other related concepts but not interpersonal sensitivity ($n = 20$), not using paranoia or a related symptom as main outcome ($n = 5$), article not written in English ($n = 2$), interpersonal sensitivity defined as the positive trait of interpersonal awareness, rather than as defined by Boyce & Parker (1989) ($n = 1$).

In total, $n = 14$ studies were selected for the systematic review. The strength of inter-rater agreement was high, (weighted $\kappa=0.86$) and disagreement was resolved through discussion of studies in relation to the inclusion criteria.

FIGURE 1 ABOUT HERE

Information extraction

Fourteen studies were included, with the earliest included study published in 1999 (Hodges et al., 1999). Two publications (Freeman et al., 2008; Freeman et al., 2008b) were linked, with one using a subsample of the other, but because they were investigating different outcomes, they will be listed as two separate studies. Twelve studies were carried out in the UK, one in Italy, and one in Iran.

The total sample size was N = 12, 138 participants. Sample sizes ranged from N = 11 (Bell and Freeman, 2014) to N = 8576 (Bebbington et al., 2013), with the median sample size of n= 90. Except for the population samples in two studies (Sharifi et al., 2012; Bebbington et al., 2013), all samples were initially self-selected. In two studies, researchers conducted selection of participants for a second experiment based on participants' initial paranoia scores (Freeman et al., 2005c; Green et al., 2011) to ensure a range of paranoia scores across the sample.

Participant age ranged from 17 years to 77 years (mean age: 28.7 years). One study (Bebbington et al., 2013) did not report the mean age, only that the sample was 'representative of the British population'. All studies had similar proportions of men and women in their samples and most participants were 'White'. IQ was reported in six studies (Freeman et al., 2005; 2005b; Valmaggia et al., 2007; Freeman et al., 2008, 2008a, 2010;), and drug use was reported in only one study (Hodges et al., 1999).

Except for one study (Bell and Freeman, 2014), which had a pre/post design, all studies were cross-sectional. Nine studies used an experimental design. Data were analysed using t-tests, Mann-Whitney-U tests, regression analyses and ANOVAs. Only three studies adjusted analyses for potential confounding variables (Freeman et al., 2005; 2008; 2008a), and one study adjusted analyses for depression only (Masillo et al., 2012). No study adjusted p-values to account for multiple testing.

Assessment of interpersonal sensitivity

The assessment of interpersonal sensitivity varied across studies (Table 1). However, all used validated measures which included questions thought to tap into the constructs in question with the most frequently used measure being the interpersonal sensitivity measure (IPSM) developed by Boyce & Parker (1989).

Of the studies using the IPSM (Boyce & Parker, 1989), six studies (Freeman et al., 2005a, 2005b; Valmaggia et al., 2007; Green et al., 2011; Masillo et al., 2012; 2016;) also reported results from subscales (interpersonal awareness, need for approval, separation anxiety, timidity, fragile inner self).

Outcomes: Trait paranoia, state paranoia and group differences in interpersonal sensitivity

In eleven studies, paranoia, ideas of reference, or ideas of persecution were the main outcome. In the remaining three studies, group differences in interpersonal sensitivity (Hodges et al., 1999; Masillo et al., 2012; 2016) were main outcomes.

TABLE 1 ABOUT HERE

Interpersonal sensitivity and trait paranoia

Clinical samples

Four studies investigated interpersonal sensitivity and trait paranoia in clinical samples (Hodges et al., 1999; Masillo et al., 2012; Bell and Freeman, 2014; Masillo et al., 2016).

Three studies used a case-control design (Hodges et al., 1999; Masillo et al., 2012; Masillo et al., 2016), and the study by Bell and Freeman (2014) used a pre-post design. Albeit different definitions of ‘cases’ and ‘controls’, and different measures of trait paranoia were used (Table 1), all three case-control studies reported significantly higher rates of interpersonal sensitivity in cases than in controls. The effect size was reported as $r = 0.24$ (small) in one study (Masillo et al., 2016). The IPSM subscales interpersonal awareness and separation anxiety were also higher in cases in the study by Masillo et al. (2016), and interpersonal awareness, separation anxiety and fragile inner self were higher in cases in the study by Masillo et al. (2012). In addition, Masillo et al. (2016) reported statistically significant correlations between interpersonal sensitivity and negative prodromal symptoms in both, cases and controls.

Bell and Freeman (2014) found significant reductions in interpersonal sensitivity, overall paranoia, ideas of reference, ideas of persecution, and persecutory delusions after an intervention targeting interpersonal sensitivity. The effect sizes were large (Green Paranoid Thoughts Scale total: $d = 1.25$, Green Paranoid Thoughts Scale reference: $d = 1.38$, Green Paranoid Thoughts Scale persecution: $d = 0.94$, PSYRATS: $d = 3.26$).

General population samples

Three studies investigated the association of interpersonal sensitivity and trait paranoia in general population samples (Freeman et al., 2005a; Bebbington et al., 2013; Sharifi et al., 2012).

Regardless of method of assessment of interpersonal sensitivity, or paranoia (Table 1), it was found in all three studies that interpersonal sensitivity was associated with paranoid thinking. Freeman et al. (2005a) reported a moderate correlation ($r = 0.47$) between the IPSM total and the Paranoia Scale (Fenigstein and Vanable, 1992), and Sharifi et al. (2012) found a strong correlation between paranoia

and interpersonal sensitivity, both assessed by the SCL90-R (Derogatis and Fitzpatrick, 2004). These associations were maintained in adjusted regression analyses using backward elimination. Bebbington et al. (2013) confirmed the exponential distribution of paranoia in the population. He identified four distinct classes in his study, with the largest class (33.3%) of the sample termed as the 'interpersonal sensitivity class'; scoring highly on interpersonal sensitivity and moderately on mistrust.

Interpersonal sensitivity and state paranoia

Clinical Samples

Two experimental studies (Valmaggia et al., 2007; Freeman et al., 2010) used a virtual reality environment to explore whether a neutral environment could elicit paranoid interpretations in participants with low paranoia, high non-clinical paranoia, and persecutory delusions (Freeman et al., 2010), or those with an at risk mental state of psychosis (Valmaggia et al., 2007).

Both, Valmaggia et al. (2007) and Freeman et al. (2010) used the State Social Paranoia Scale as main outcome measure to assess paranoia, and the IPSM (Boyce and Parker, 1989) to assess interpersonal sensitivity. In both studies, samples were self-selected. Freeman et al (2010) matched the clinical sample with a non-clinical sample on some demographic variables such as gender.

Freeman et al. (2010) reported a linear association between increasing levels of paranoia and interpersonal sensitivity. However, in an ordinal regression analysis which considered all variables investigated together (anxiety, worry, interpersonal sensitivity, depression, total number of anomalous experiences, beads drawn, and number of traumatic events), only anxiety and number of traumatic events remained significant.

Valmaggia et al. (2007) found that there was no correlation with persecutory ideation and overall IPSM score ($r = 0.16$ $p = 0.504$); although the IPSM subscale fragile inner self was significantly moderately correlated with persecutory ideation ($r = 0.46$, $p = 0.049$).

General population samples

Five studies investigated the association of interpersonal sensitivity and paranoia in general population samples using an experimental design (Freeman et al., 2003; 2005a, 2008a; 2008b; Green et al., 2011). Four studies used virtual reality to investigate associations with paranoia Freeman et al., 2003; 2005a, 2008a; 2008b); whereas Green et al. (2011) used a 'real world scenario' with stooges.

Paranoia was assessed differently across studies (Table 1). Green et al. (2011) reported no significant difference in total IPSM score in those who made paranoid attributions and those who did not, but found a significant difference between groups in levels of separation anxiety ($U = 131$, $p = 0.05$). In contrast, Freeman et al. (2008) and Freeman et al. (2008b) found that overall IPSM score was associated with state paranoia. The association found in the latter study was maintained in adjusted analyses, whereas the former study did not adjust analyses for potential confounders. Neither study reported results on any of the subscales. Freeman et al. (2003) found that higher levels of BSI-Interpersonal sensitivity was associated with higher levels of perceived persecution in VR. This finding was maintained in adjusted analyses. Freeman et al. (2005b) found no significant correlation in IPSM and the VR-persecution score. However, the authors reported that the IPSM subscale timidity was significantly correlated with VR-persecution ($r = 0.47$, $p = 0.009$); other subscales were not significantly correlated with VR-persecution.

DISCUSSION

Findings from this systematic review demonstrate a robust association between interpersonal sensitivity and paranoia in clinical and general population samples alike, regardless of method of assessment of both paranoia and interpersonal sensitivity.

Studies in this review were all 'moderate' or 'good' quality; largely owing to the large number of experimental studies included. Observational studies had large sample sizes and robust methodologies, giving confidence in the finding that paranoia is associated with interpersonal sensitivity. Although this finding was more pronounced in studies of trait paranoia, it nevertheless suggests that interpersonal sensitivity is a construct which warrants further empirical and clinical attention.

It is likely that the discrepancy of findings observed in studies of trait and state paranoia are due to differences in purpose of the studies, and thus, differences in sampling and measurement. Studies which used state paranoia as an outcome were exclusively experimental, and primarily concerned with establishing the feasibility of using a VR environment to study paranoia, with the state paranoia measure having been developed for this specific purpose. Therefore, questions were fewer and less comprehensive than those investigating trait paranoia. Samples were less likely to be representative of the general population, whereas studies investigating trait paranoia were usually representative or well matched on potential confounders like age, gender and social economic status. The difference in

purpose of the studies investigating state and trait paranoia also raises the question whether these studies were sufficiently powered to detect associations with interpersonal sensitivity or its related constructs in these studies.

Finally, since the primary purpose in studies using state paranoia was not the investigation of interpersonal sensitivity but the feasibility of using a VR environment to investigate paranoia, interpersonal sensitivity was not measured concurrently with state paranoia in any of the studies; making it difficult to ascertain whether any lack of association was due to fluctuations in those variables, or whether state and trait paranoia, albeit highly correlated, measure slightly different underlying constructs which relate differently to interpersonal sensitivity.

Taken together, it is likely that using measures of state paranoia may not be the ideal route to answering the question whether interpersonal sensitivity is associated with paranoia, and using a measure of trait paranoia in future studies may prove more fruitful.

From a theoretical perspective, findings from this review strengthen the hypothesis that feelings of personal vulnerability and exaggerated socially evaluative concerns are central for both, onset and maintenance of paranoid symptoms; in line with Freeman's (2007) theory that paranoia builds directly on these feelings. Findings from our review therefore support and expand those from two recent systematic reviews on self-esteem and self-concepts more widely (Kesting and Lincoln, 2013; Tiernan et al., 2014), which both concluded that there is little empirical support for the idea that paranoia serves to protect self-esteem, as proposed by Bentall et al. (2001), but that specific negative schemas about the self significantly contribute to the development of paranoia. Findings from our review suggest that interpersonal sensitivity may be an important mediator in the pathway from negative self-schemas to paranoia, although this hypothesis will need to be tested in future research.

In this context, it will also be interesting to begin to understand better when, and how precisely interpersonal sensitivity develops. There have been suggestions that adverse interpersonal experiences, such as childhood trauma (Fisher et al., 2012), bullying victimization (Butler et al., 2007), and discrimination (Stowkowy and Addington, 2012) may be significantly implicated in the formation of negative beliefs about the self. However, to date, the mechanisms whereby these experiences then convert to interpersonal sensitivity are not well understood. Although there are emerging longitudinal studies to suggest a unidirectional pathway from negative self-schemas more broadly to paranoia (Fowler et al., 2012; Oliver et al., 2012; Jaya et al., 2017), the role of interpersonal sensitivity in these pathways has not been investigated. A recent study has shown that interpersonal sensitivity mediated the association between childhood bullying victimisation and paranoia (McDonnell et al., 2017), but

because the design was cross-sectional, causality could not be established. Further longitudinal research will therefore be vital to elucidate the role of interpersonal sensitivity in paranoia.

Similarly, it is not yet clear whether interpersonal sensitivity is indeed as stable and resistant to change as suggested in the definition by Boyce & Parker (1989). Tentative evidence from the study by Bell and Freeman (2014) included in this review suggests that interpersonal sensitivity may be more amenable to intervention than would be expected from an enduring 'personality trait'. However, since this study was a pilot with significant limitations, such as the lack of a control group and a small, selected sample, it is at this stage not possible to draw firm conclusions about the malleability of interpersonal sensitivity.

The systematic review by Kesting and Lincoln (2013) noted that there was some support for the hypothesis that fluctuations in self-esteem, rather than self-esteem per se, are important in the development of paranoia. Indeed, findings from our review also point tentatively towards the idea that the perceived fragility of the self, as measured by the IPSM subscale 'fragile inner self', possibly reflected in fluctuations in self-esteem, may deserve closer attention when considering the development of paranoia. Although only two studies included in this review reported on this link, since this review was conducted, a further study has been published which found that the IPSM subscale 'fragile inner self' was significantly associated with paranoid ideation in a sample of adolescents seeking help for psychological problems (Masillo et al., 2017).

It is noteworthy that trying to define perceptions of the self in relation to others, and its association with paranoia is an area of considerable complexity. Whereas previous work has predominantly focused on elucidating the role of self-esteem and self-worth more globally (Kesting and Lincoln, 2013), it appears now timely to begin parsing out more fine-grained concepts that make up the interpersonal difficulties observed in people with psychosis. The IPSM (Boyce and Parker, 1989) with its subscales of interpersonal awareness, fragile inner self, need for approval, separation anxiety, and timidity may offer a comprehensive measure of interpersonal difficulties for this purpose. Using a validated, established measure across studies and samples would be beneficial to allow for meaningful comparisons; leading to firmer conclusions on the role of interpersonal sensitivity and its related constructs in psychosis. This would also help to identify future clinical targets.

Clinically, findings from this review suggest that it will be important to consider the impact of interpersonal sensitivity on paranoid symptoms, and how this finds expression within interpersonal relationships, including the therapeutic relationship. This may be of importance since there is now evidence to suggest that the therapeutic relationship is a crucial factor in the success of therapeutic intervention for psychosis (Goldsmith et al., 2015).

Refining our understanding about how interpersonal sensitivity and its constructs are related to paranoia could help to design specific, targeted interventions to individuals suffering from high interpersonal sensitivity before they show symptoms of psychosis. The use of virtual reality therapeutically could give an opportunity to work on interpersonal experiences under controlled conditions. Indeed, there have been some successful trials of VR for treatment of social anxiety (Anderson et al., 2013; Bouchard et al., 2017). It is conceivable that similar approaches could be developed for interpersonal sensitivity. There is also emerging evidence that compassion-focused approaches could provide a promising route to enhancing specific, dysfunctional aspects of self-esteem in clients with paranoia (Lincoln et al., 2013; Ascone et al., 2017). To date, there has only been one pilot study of a targeted intervention for interpersonal sensitivity (Bell and Freeman, 2014), with encouraging results. However, these findings were in a severely impaired clinical sample and will need to be replicated in a larger sample with a broader set of characteristics to begin building the evidence base for targeted prevention of, and early intervention in psychosis.

Limitations of the review

This review has some limitations. We only included published literature which may have introduced some publication bias. Search criteria were fairly narrow which may have precluded inclusion of studies which investigated wider constructs related to interpersonal sensitivity or psychosis. However, as discussed above, two recent reviews have explored the role of self-esteem, and self-concepts in paranoia (Kesting and Lincoln, 2013; Tiernan et al., 2014), and therefore we thought it important to hone in on the literature on interpersonal sensitivity, specifically.

CONCLUSIONS

This systematic review of 14 studies with a total of 12,138 participants showed a clear association between interpersonal sensitivity (encompassing interpersonal awareness, a fragile inner self, need for approval, separation anxiety and timidity) and paranoia. Although this research area is considerably complex, and many questions remain, results nevertheless suggest that interpersonal sensitivity a construct which warrants further empirical and clinical attention. Refining our understanding about the specific interpersonal difficulties experienced by individuals with paranoia could help to design specific, targeted interventions to individuals suffering from high interpersonal sensitivity before they show symptoms.

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CONFLICT OF INTEREST

None.

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Figure 1: PRISMA flow diagram

PRISMA 2009 Flow Diagram

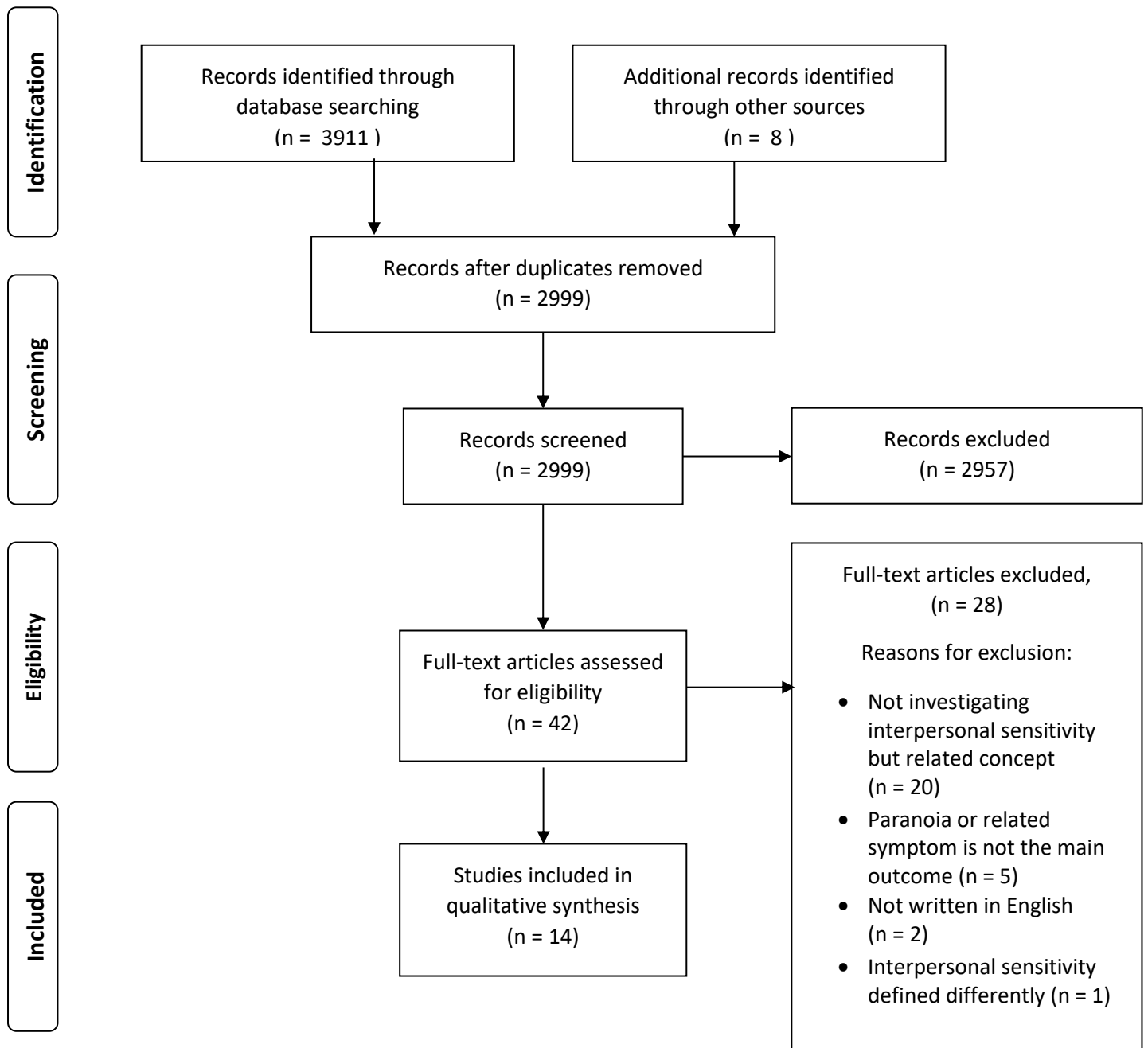


Table 1. Summary and quality assessment of included studies

Author (year)	Study design	Sample	Sample selection	Main outcome Paranoia Measure	Interpersonal sensitivity measure	If IPSM used, reporting on subscales?	Main findings	Quality rating
Interpersonal sensitivity and trait paranoia in clinical samples								
Bell & Freeman (2014)	Pre-post design (CBT intervention for interpersonal sensitivity)	N = 11 patients with persecutory delusions Age: (Mean, SD) = 38.0 y (15.8) Male Gender: n = 5 White Ethnicity: n = 9 diagnoses were schizophrenia (n = 6), delusional disorder (n = 1) and unspecified psychosis (n = 4). Medication: n = 10	self-selected inclusion criteria: experiencing for at least six months a current persecutory delusion as defined by Freeman and Garety (2000); a rating of delusional conviction over 50% certainty; reporting interpersonal sensitivity, defined as a score on the IPSM (Boyce & Parker, 1989) of 95 or higher; aged between 18 and 65 years; a case note ICD-10 diagnosis of schizophrenia, schizoaffective disorder, or delusional disorder or individuals with no diagnosis but where psychosis was judged by the team to be the primary problem; and stable medication dosage for at least a	Trait paranoia Green Paranoid Thought Scale (Green et al., 2008) Other measures: Psychotic Symptoms Rating Scale: delusions subscale (Haddock et al., 1999)	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	NO	significant decrease in interpersonal sensitivity as assessed by the IPSM from pre-therapy to post-therapy. The effects size was large. There were also significant reductions on all five visual analogue scale items assessing interpersonal sensitivity. significant decrease between pre-therapy and post-therapy in the level of overall paranoia (GPTS total), ideas of reference (GPTS: A), ideas of persecution (GPTS: B) (and persecutory delusions (PSYRATS). A Pearson's product-moment correlation indicated that change on the IPSM (mean pre- and post-therapy difference)	good

period of 1-month prior to taking part in the study. Exclusion criteria were: inability to give informed consent; the patient not wanting help for interpersonal sensitivity; substance dependence as the primary problem; already being in receipt of psychological therapy; organic impairments or a learning disability; and insufficient understanding of the English language for meaningful participation.

was positively correlated with change on the GPTS (mean pre- and post-therapy difference), though this association did not reach statistical significance

Hodges et al (1999)	Observational (Prospective)	N = 130 n = 100 High risk of schizophrenia n = 30 HC Age: (Mean, SD) HR= 21.6 y (2.8), HC = 21.1 y (2.2) Male Gender: HR = 52, HC = 15 Single: HR = 75, HC = 27	HR: aged between 16-25 at least 2 members of family suffered from schizophrenia, identified by examining case notes HC recruited through index cases. HC matched to cases	Trait paranoia Structured interview for Schizotypy (SIS; Kendler et al., 1989)	Structured interview for Schizotypy (SIS; Kendler et al., 1989)	Not used	The groups in our study show significant differences in some of the parameters in the SIS, namely the high-risk group complained of increased interpersonal sensitivity, social isolation and suicidal preoccupation and demonstrated	fair
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		Higher education: HR = 35, HC = 15 Unemployed: HR = 17 , HC = 4 Heavy Alcohol use: HR = 13, HC = 4 Cannabis and other drug use: HR = 32 HC = 8					increased oddness, restricted affect and more disorganisation of speech.
Masillo et al (2016)	Cross- sectional (survey)	Originally N = 147 screened; then divided into n = 39 UHR, n = 108 not UHR UHR sample: 26 (66.7 %) individuals were under 18 years old NUHR sample: 67 (62 %) were under 18 years of age. Age: (Mean, SD) UHR= 17.36y (5.5), NUHR = 18.51 y (6.26) Male Gender: UHR = 21, NUHR = 48 unemployed: UHR= 8, NUHR = 29	Recruitment through primary care, school and university counselling, justice system youth accommodation centres, self-referrals Inclusion criteria: age between 12 and 35 years; IQ ≥70; sufficient knowledge of the Italian language; the disorder is not secondary to or correlated with a general medical condition; willingness and ability to provide free written informed consent (the informed consent was provided by parents or guardian in case of minors).	Main outcome: Trait paranoia Prodromal Questionnaire, (PQ; Loewy et al., 2005)	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	YES	Higher IPSM total score, fair interpersonal awareness and timidity in UHR samples. A statistically significant correlation was also found between timidity IPMS subscale and PQ negative subscale in the NUHR sample Significant positive correlation between interpersonal sensitivity, separation anxiety, and fragile inner self and prodromal symptoms of paranoia in UHR group

Senior high school
education: UHR =
9, NUHR = 35

Masillo et al (2012)	Cross- sectional (survey)	N = 101 n= 62 at risk mental state for psychosis n = 39 healthy control Age: (Mean, SD) : ARMS= 22.6 y (4.5), HC = 24.0 y (4.2)) Male Gender: ARMS = 37, HC = 20 White Ethnicity: ARMS = 21, HC = 15 Single: ARMS = 46, HC = 22 unemployed: ARMS = 36, HC = 3	self-selected ARMS recruited through 1 site (OASIS) ARMS was evaluated using the Comprehensive Assessment of At-Risk Mental States Healthy controls matched for geographic region and ethnicity as ARMS. The following inclusion criteria for HC were used: participants aged between 18 and 35 years, lived (or grew up) in South London, and no personal history of mental health problems.	Trait paranoia Prodromal Questionnaire (Loewy et al. 2005),	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	YES	statistically significant differences between groups in IPSM total score, interpersonal awareness, separation anxiety, and fragile inner self. Higher sensitivity to interpersonal interactions, anxiety about separation from significant others and sense of having an inner or core self that is unlikeable and needs to be hidden from others were all associated with higher numbers of positive prodromal symptoms. The higher the interpersonal awareness, separation anxiety, fragile inner self, and total IPSM scores among ARMS clinical risk participants, the higher the level of paranoid ideas and suspiciousness. A	fair
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significant association between separation anxiety subscale score and paranoid/suspiciousness was also found among control participants. The degree of association between IPSM total scores and PQ positive symptoms subscale scores were no longer statistically significant after controlling for depression.

Interpersonal sensitivity and trait paranoia in general population samples

Bebbington et al (2013)	Observational (Cohort)	N = 8576 aged 18-74 representative sample of the British population from the second British National Psychiatric Morbidity Survey	A total of 15 804 addresses were obtained. Interviewers visited these to identify private households with at least one person aged 16-74 years. One person was selected from each qualifying household using the Kish grid method. ²¹ Just under 70% of those approached agreed to a first phase interview, which the vast majority completed in full, providing 8576	items 2, 3, 3a and 3b from the PSQ, relating to ideas of persecution, conspiracy and interference. From the SCID-II, we used items 2, 3, 4, 6, 10, 25, 26, 27, 28, 33 and 35.	From the SCID-II, we used items 2, 3, 4, 6, 10, Community 1 (Interpersonal sensitivities)	Not used	The largest class comprised 33.3% of the sample, and as a group its members scored highly on interpersonal sensitivity and moderately on mistrust: it is best described as the interpersonal sensitivity class.	good
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individuals for the current analysis.								
Freeman et al (2005a)	Cross-sectional (survey)	N = 327 students, exclusion: mental illness Mean age (SD): 22.6 y (5.9), Median: 21 Mean IQ (SD): 104.6 (12.0), range 69-133 Male Gender: n = 100 White Ethnicity: n = 243	Self-selected	Trait paranoia Paranoia Scale (Fenigstein & Vanable, 1992) Other measures: Peters Delusions Inventory (Peters et al., 1999)	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	YES	The final model had an adjusted R ² of .44 and, in addition to age, sex, and ethnicity, contained the following predictors: IPSM-separation anxiety, DASS-depression, hallucinations, IPSM-fragile inner self and NFC-decisiveness	fair
Sharifi et al (2012)	Observational (Cohort)	N = 2,158, aged 18-65	Population-based cross-sectional study in Tehran, Iran The sampling method was a two-stage random sampling from the households in the area. In the first stage, 5 out of 8 districts located in the area of the research centre were selected by simple random sampling. In the	Trait paranoia Symptom Checklist-90-Revised (SCL-90-R)	Symptom Checklist-90-Revised (SCL-90-R)	Not used	Both SCL-90-R dimensions of psychosis were correlated with age, stressful life events and the dimensions of depression, anxiety, phobic anxiety, somatization, hostility, obsessive-compulsive symptoms and interpersonal sensitivity	good

second stage, 2,158 people from the selected age range living in the 5 districts were recruited to the study and interviewed by systematic random sampling. If the selected participant was not present in the house or unable to provide a coherent interview, the interviewer left for the next dwelling. The refusal rate was low, at 4%.
 Age: (Mean, SD) :33.17 y (12.45)
 Male Gender: 45.3%
 Single:30.3%
 Unemployed: 11%

Interpersonal sensitivity and state paranoia in clinical samples

Freeman et al (2010)	Experimental	Total sample: N = 90; low paranoia (LP; n= 30) high nonclinical paranoia (HP; n= 30); persecutory delusions group	Self - selected	State paranoia State Social Paranoia Scale (Freeman et al, 2007) Other measures: Trait paranoia	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	NO	Increasing levels of paranoia (SSPS) associated with increasing levels of anxiety, depression, interpersonal sensitivity, anomalies of	good
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(PD; n = 30)
non-clinical groups
matched w clinical
group for sex and
marital status
Age: (Mean, SD) :
LP = 44.2 y (11.2),
HP = 36.0 y (11.7),
PD = 44.2 (11.7)
Mean IQ (SD): LP =
101.8 (15.2), HP =
98.3 (14.5), PD =
91.2 (11.2)
Male Gender: LP =
18, HP = 18, PD =
18
White Ethnicity: LP
= 25, HP = 23, PD =
16
Single: LP = 27, HP
= 28, PD = 27
No degree/GCSE :
LP = 10, HP = 5, PD
= 16
Long-term
unemployed/never
worked: LP = 7, HP
= 6, PD = 22
Computer game
use: LP = 20, HP =
16, PD = 17

Green et al.
(2008)
Paranoid
Thoughts
Scale

experience and number
of traumatic events.
In ordinal regression
model, only predictors
of paranoia spectrum
were anxiety,
anomalous experiences

Valmaggia et al (2007)	Experimental	<p>n = 21 ARMS</p> <p>All participants were aged between 16 and 35 years, had never experienced a psychotic episode, and were being managed clinically by OASIS in the community. Participants assessed with a detailed clinical assessment using the Comprehensive Assessment of the At-Risk Mental State with interview</p> <p>Age: (Mean, SD): 25.0 y (4.7)</p> <p>Male Gender: 13</p> <p>White Ethnicity: 12</p> <p>Single: HR = 75, HC = 27</p> <p>Unemployed: 7</p> <p>Premorbid IQ (NART) = 98.4 (8.8)</p> <p>Attenuated symptoms: 14</p>	self-selected	<p>State paranoia Virtual Reality Questionnaire (Freeman et al, 2005)</p> <p>Three subscales: VR persecution, VR neutral, VR positive)</p> <p>Other measures:</p> <p>Trait paranoia Green et al Paranoid Thoughts Scale (Green et al., 2008), Paranoia Scale (Fenigstein & Venable, 1992)</p>	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	YES	Overall interpersonal sensitivity not associated with VR-Paranoia, but fragile inner self correlated with VR-paranoia	good
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Interpersonal sensitivity and state paranoia in general population samples								
Freeman et al (2008) a)	Experimental	N = 200 Mean age (SD): 37.5 y (13.3), range 18-77 Mean IQ (SD): 104.6 (12.0) range 69-133 Male Gender: n = 100 White Ethnicity: n = 135 No degree/GCSE : n = 50 Long-term unemployed/never worked: n = 33 Computer game use never: n = 101	Self-selected general population sample, representative of the local adult population	State paranoia State Social Paranoia Scale (Freeman et al, 2007) Other measures: Trait paranoia Green et al. (2008) Paranoid Thoughts Scale Part B	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	NO	There was a significant association between trait levels of paranoia and the occurrence of persecutory thinking in virtual reality. Individuals who reported paranoid thoughts in day-to-day life were about twice as likely to experience persecutory thoughts in virtual reality compared with individuals who reported no paranoid thoughts in day-to-day life.	fair
Freeman et al (2008) b)	Experimental	N = 200 Mean age (SD): 37.5 y (13.3), range 18-77 Mean IQ (SD): 104.6 (12.0) range 69-133 Male Gender: n = 100 White Ethnicity: n = 135	Self-selected general population sample, representative of the local adult population Exclusion criteria: a history of severe mental illness (e.g. schizophrenia, bipolar disorder, affective psychosis) were	State paranoia State Social Paranoia Scale (Freeman et al, 2007)	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	NO	Anxiety, depression, worry and interpersonal sensitivity all had similar, significant associations with paranoia and social anxiety	fair

		No degree/GCSE : n = 50 Long-term unemployed/never worked: n = 33 Computer game use never: n = 101	excluded from the study. Individuals with a history of epilepsy					
Freeman et al (2005) b)	Experimental	N = 30 Age: (Mean, SD) = 22 y (5), Median: 21 Male Gender: n = 15 White Ethnicity: n = 21	Originally self-selected then researcher selected based on PS score. Participants were selected across paranoia spectrum.	State paranoia Paranoia in VR questionnaire Social anxiety in VR questionnaire Other measures: State paranoia Paranoia Scale (Fenigstein & Venable, 1992)	Interpersonal Sensitivity Measure (Boyce & Parker, 1989)	YES	Persecutory ideation in virtual reality was predicted by higher levels of paranoia, anxiety, timidity, hallucinatory experiences, and sense of presence. Social anxiety in VR correlated with interpersonal awareness, interpersonal sensitivity, and separation anxiety	fair
Freeman et al (2003)	Experimental	N = 24 HC without history of mental illness Age: (Mean, SD) = 26 y (6) Male Gender: n = 12 Students: n = 21, admin staff: n = 3	Self-selected	Paranoia in VR questionnaire Other measures Trait paranoia Paranoia Scale (Fenigstein & Venable, 1992) Brief symptom inventory	Brief Symptom Inventory (Derogatis, 1993)	Not used	Higher levels of interpersonal sensitivity and anxiety were associated with higher levels of persecutory ideation in virtual reality. Only BSI-Interpersonal Sensitivity remained significant in the	fair

				(Derogatis, 1983)			adjusted regression analysis	
Green et al (2011)	Experimental	First, N = 323 Then N = 58 The inclusion criteria for completing the survey were adults aged 18–65, English as a first language, and normal or corrected-to- normal hearing. The main exclusion criterion was a history of mental illness. Age: (Mean, SD) = 29.7 y (11.5), range 18-65 Male Gender: n = 27 White Ethnicity: n = 41 GCSE highest level of Education: n = 4 Students: n = 30	First, a sample of adults (N = 323) from both the local community and King's College London were recruited via email and local advertisement to complete an online survey that comprised two trait measures of trait paranoia: the Paranoia Scale (PS), Fenigstein and Venable (1992) and the Green et al. Paranoid Thoughts Scale (GPTS), Green et al., 2008 Then N = 70 were selected based on GPS scores accross the paranoia continuum and n= 58 chose to take part	State paranoia explanation of event Other measures: Green Paranoid Thoughts Scale (Green et al., 2008, Paranoia Scale (Fenigstein & Venable, 1992)	Interpersonal Sensitivity Measure (Boyce & Parker, 1989),	NO	significant difference was noted between the groups in levels of separation anxiety, with those making paranoid attributions showing higher levels of separation anxiety. Overall interpersonal sensitivity not significantly associated with paranoid explanations.	fair

Abbreviations: CBT = Cognitive Behavioural Therapy; GCSE = General Certificate of Secondary Education; GPTS = Green Paranoid Thoughts Scale; ICD-10: International Statistical Classification of Diseases and Related Health Problems; IQ = Intelligence Quotient; HC = Healthy Control; HR = High Risk; NART = National Adult Reading Test;

NUHR = Not ultra high risk; OASIS = Outreach and support in South London; PSYRATS = Psychotic Symptoms Rating Scales; SD= Standard Deviation; UHR = Ultra high risk; VR = Virtual Reality